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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	GOLD ET AL.	)
		)
SERIAL NO.:	10/037,986	) EXAMINER: FORMAN, B.J.
		)
FILED:	OCTOBER 18, 2001	) ART UNIT: 1634
		)
FOR:	NUCLEIC ACID LIGANDS	) CONF. NO.: 1060

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

In regard to the referenced application, Appellants submit this Appeal Brief.

I. REAL PARTY IN INTEREST

The real party in interest is Gilead Sciences, Inc. The right of Gilead Sciences, Inc. to take action in the subject application was established by virtue of the following chain of title:

1. An assignment from the inventors to University Research Corporation, recorded at Reel 6329, Frame 0386, filed in predecessor application serial no. 07/714,131, filed June 10, 1991.

2. An assignment from the University Research Corporation to NeXstar Pharmaceuticals, Inc., recorded at Reel 8119, Frame 0541, filed in predecessor application serial no. 07/714,131.

3. An assignment from NeXstar Pharmaceuticals, Inc. to Gilead Sciences, Inc. recorded at Reel 012872, Frame 0364.

II. RELATED APPEALS AND INTERFERENCES

The undersigned legal representative of Appellant hereby confirms that there are no known appeals or interferences relating to the present application, or any parent application, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Claims 2 and 4-8 are pending in the application and claims 1 and 3 have been cancelled. No claims have been allowed. Claims 2 and 4-8 stand rejected under a final Office Action mailed January 16, 2004. The rejections of each of claims 2 and 4-8 are being appealed.

IV. STATUS OF THE AMENDMENTS

In response to the final Office Action of January 16, 2004 (referred to herein as "Office Action"), Appellants filed an Amendment and Remarks of June 16, 2004 which amended claims 2 and 5 and added new claims 9-12. Appellants received an Advisory Action dated July 13, 2004, which indicated that the amendments and new claims had not been entered. The claims set forth in Section VIII reflect the fact that the amendments and new claims submitted on June 16, 2004, have not been entered.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The subject invention comprises a method for identifying a nucleic acid binding protein's binding site on a region of a DNA or RNA. The broadest claim, claim 2, is directed to a method that involves adding a nucleic acid ligand to a nucleic acid binding protein and the DNA/RNA region, and determining whether the nucleic acid ligand inhibits the binding protein from binding to the RNA/DNA region. The inhibitory nucleic acid ligand, by virtue of its sequence and/or structure, assists in the identification of the binding site in the DNA/RNA region. This method is described in the substitute specification at page 25, lines 11-17; page 41, lines 13-22; page 42, line 25 to page 43, line 3; page 47, lines 7-9; page 49, line 15 to page 52, line 13; and Examples 1, 3 and 13.

The nucleic acid ligand used in the claim 2 method can be made by the method of

claim 4. This method comprises: (a) contacting a candidate mixture of nucleic acids each of which have a randomized sequence with the binding protein, whereby nucleic acids having an increased affinity to the protein relative to the candidate mixture may be partitioned from the remainder of the candidate mixture; (b) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture; and (c) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids, whereby a nucleic acid ligand of the protein may be identified. This method is described in the substitute specification at page 7, line 25 to page 9, line 27; and page 19, line 27 to page 21, line 1.

The binding site in the DNA/RNA region can be a promoter, an origin of replication, a ribosomal binding site and/or a tRNA binding site (claim 5), as described on page 41, lines 13-22 of the substitute specification. The binding protein can regulate transcription (claim 6, Example 12) or translation (claim 7, pages 49-52; and Examples 1 and 13). The binding proteins can be transcriptional activators, transcriptional repressors, transcription complexes at promoter sites, replication accessory proteins, DNA polymerases, RNA polymerases and translational repressors (claim 8, page 41, lines 13-22, and Examples 2 and 3 of the substitute specification).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 2 and 4-8 stand rejected under 35 USC §112, first paragraph, for lack of adequate written description.

Claims 2, 3 and 5-8 stand rejected under 35 USC §102(b) over Giordano *et al.*, U.S. Pat. No. 5,859,227.

Claims 2, 3, 5, 6 and 8 stand rejected under 35 USC §102(b) over Weissman *et al.*, U.S. Pat. No. 5,861,246.

Claim 4 stands rejected under 35 USC §§ 102(b)/103 over Weissman *et al.*, U.S. Pat. No. 5,861,246.

VII. ARGUMENT

A. The Rejection of Claims 2 and 4-8 under 35 USC § 112, First Paragraph

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 112, First Paragraph Written Description Requirement

The established rule in relation to the Section 112, written description requirement is that the claimed invention is adequately described if the specification reasonably conveys to persons skilled in the art that the inventors invented or were in possession of the claimed subject matter as of the filing date of the application (*In re Wertheim*, 541 F.2d 257,262, 191 USPQ 90, 97 (CCPA), *appeal after remand*, 646 F.2d 527, 209 USPQ 554 (CCPA 1981); *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000), *cert. denied*, 121 S. Ct. 1167 (2001)). The claimed subject matter need not be described *in haec verba* in the specification in order for the written description requirement to be fulfilled (*Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000)).

The burden is upon the Patent Office to establish a *prima facie* case that the written description requirement has not been met. The Examiner has the initial burden of presenting reasons or evidence supporting his/her position that the skilled artisan would not recognize the claimed invention in the specification (*Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (BPAI 1987) (citing *In re Wertheim*, 541 F.2d 257, 192 USPQ 90 (CCPA 1976)).

If a *prima facie* case of lack of written description is established, the Appellants can rebut such case by evidence that shows that the application does in fact include an adequate written description of the invention (*In re Marzocchi*, 439 F.2d 220, 223-4, 169 USPQ 367, 369 (CCPA 1971)).

2. The Rejection of Claims 2 and 4-8 under 35 U.S.C. § 112, first paragraph is improper

The Appellants respectfully submit that the Section 112, first paragraph, lack of written description, rejection is improper because the Examiner has not established a

prima facie case of lack of written description. In the alternative, Appellants argue that assuming *arguendo*, that *prima facie* lack of written description had been established, it is rebutted by experimental evidence that the specification adequately describes the claimed invention.

The Examiner's position appears to be based on the following points:

(i) There is no actual or literal description in the specification for independent claim 2 (Office Action, page 5, paragraph 2):

> 2. A method for identifying a nucleic acid binding protein's binding site on a region of a DNA or RNA comprising:
> a) providing a nucleic acid ligand to the nucleic acid binding protein;
> b) adding said nucleic acid ligand to said nucleic acid binding protein and said DNA or RNA region; and
> c) determining whether said added nucleic acid ligand inhibits said protein from binding to said RNA or DNA region, whereby the sequence or structure of said inhibitory nucleic acid ligand assists in the identification of the binding site in the DNA or RNA region.

(ii) Any description that is present merely suggests the foregoing method. In particular, none of the examples teach how a nucleic acid ligand can have sequence and/or structure information that is informative about the binding site on the RNA or DNA (Office Action, page 5, paragraphs 3 & 4).

Appellants contend that the Examiner has not established a *prima facie* case of lack of written description under Section 112, first paragraph, because there is literal support in the specification for the claims.

As stated above in Section VII.A, it is not necessary that the specification provide literal support (*in haec verba*) for a claim in order for the claim to meet the written description requirement (*Purdue Pharma L.P.*, 56 USPQ2d at 1483). However, the Applicants submit that each of the elements of claims 2 and 4-8 does have literal support in the specification.

"A method for identifying a nucleic acid binding protein's binding site on a region of a DNA or RNA" of claim 2 finds literal support in the following passages. At page 25, lines 11-17, the substitute specification provides:

> The method of the present invention [was] developed in connection with investigations of translational regulation in bacteriophage

> T4 infection. Autoregulation of the synthesis of certain viral proteins, such as the bacteriophage T4 DNA polymerase (gp43), involves binding of the protein to its own message, blocking its translation. The SELEX method was used to elucidate the sequence and structure requirements of the gp43 RNA binding site. SELEX allowed the rapid selection of preferred binding sequences from a population of random nucleic acid sequences. [emphasis added]

At page 41, lines 13-22 of the substitute specification, it is stated:

> The method of the present invention has multiple applications. The method can be employed, for example, to assist in the identification and characterization of any protein binding site for DNA or RNA. Such binding sites function in transcriptional or translational regulation of gene expression, for example as binding sites for transcriptional activators or repressors, transcription complexes at promoter sites, replication accessory proteins and DNA polymerases at or near origins of replication and ribosomes and translational represssors at ribosome binding sites. Sequence information of such binding sites can be used to isolate and identify regulatory regions bypassing more labor-intensive methods of characterization of such regions. Isolated DNA regulatory regions can be employed, for example, in heterologous constructs to selectively alter gene expression. [emphasis added]

At page 42, line 25 to page 43, line 3 provides:

> A number of proteins are known to function via binding to nucleic sequences, such as regulatory proteins which bind to nucleic acid operator sequences. The known ability of certain nucleic acid binding proteins to bind to their natural sites, for example, has been employed in the detection, quantitation, isolation and purification of such proteins. The methods of the present invention related to the use of nucleic acid antibodies are not intended to encompass the known binding affinity between nucleic acid binding proteins and nucleic acid sequences to which they are known to bind. However, novel, non-naturally-occurring sequences which bind to the same nucleic acid binding proteins can be developed using SELEX. It should be noted that SELEX allows very rapid determination of nucleic acid sequences that will bind to a protein and, thus, can be readily employed to determine the structure of unknown operator and binding site sequences which sequences can then be employed for applications as described herein. [emphasis added]

Step (a) of claim 2, "**providing a nucleic acid ligand to the nucleic acid binding protein,**" finds literal support at page 47, lines 7 to 9 of the substitute specification:

> The methods of the present invention are useful for obtaining

> nucleic acids which will inhibit function of a target protein, and are particularly useful for obtaining nucleic acids which inhibit the function of proteins whose function involves binding to nucleic acid . . . . [emphasis added]

Steps (b) and (c) of claim 2, "**adding said nucleic acid ligand to said nucleic acid binding protein and said DNA or RNA region; and determining whether said added nucleic acid ligand inhibits said protein from binding to said RNA or DNA region, whereby the sequence or structure of said inhibitory nucleic acid ligand assists in the identification of the binding site in the DNA or RNA region,**" also find literal support in the specification. The below passages describe the selection of nucleic acid ligands to gp43 (T4 DNA polymerase), wherein the ligands inhibit binding and polymerase function of gp43 and demonstrate homology or identity to the wild-type operator sequence for gp43.

> The template [candidate sequence] was constructed . . . to encode most of the wild-type operator sequence, except for the loop sequence. The eight base loop sequence was replaced by a randomized sequence region which was synthesized to be fully random at each base. (page 50, lines 11-14).
>
> All three independent SELEX procedures [to the gp43 target] . . . gave similar apparent consensus sequences. (page 51, lines 17-19).
>
> The wild-type sequence AAUAACUC and the loop AGCAACCU were present in approximately equal amount in the selected RNA of experiment B. The other selected variants were 1 base mutants of the two major variants. . . . [A] rough correlation between bonding affinity of an RNA [ligand] for gp43 and the abundance of the selected sequence was observed. The two major loop sequence variants showed approximately equal binding affinities for gp43. (page 52, lines 3-10).
>
> The loop sequence variant RNAs isolated by the [SELEX] selection/amplification process . . . can all act as inhibitors of gp43 polymerase activity as has been demonstrated for the wild-type operator sequence. (page 52, line 11-13).

The foregoing passages indicate that nucleic acid ligands to target gp43 obtained via the SELEX method, were effective in inhibiting the gp43 from binding to the wild-type operator on the transcript, thereby stopping gp43 polymerase activity. The inhibiting ligands had homology or identity to the wild-type operator.

The Examiner has found this written description unacceptable because the gp43 wild-type operator sequence had already been determined by prior art methods, and that

therefore the ligand competition method added nothing to that which was already determined by the prior art methods. Appellants respectfully submit that the fact that the gp43's wild-type operator sequence was determined using prior art methods, takes nothing away from the ability of the inhibitory nucleic acid ligands to a DNA/RNA binding protein to be informative about the identity or sequence of the wild-type binding site for the binding protein.

The Examiner has also argued that any written description that is present is not literal support, and at most provides only a suggestion of the claimed method. In particular, the Examiner states on page 5, fourth paragraph, of the final Office Action, that it is not sufficient that the specification provides only that the ligand "can be" useful in identifying the binding site on the DNA/RNA because the inhibitory ligand's sequence "can be" similar to the binding site on the wild-type DNA/RNA. Passages using the "can be" language are found in the above excerpts from page 41, lines 13-22; and page 42, line 25 to page 43, line 3 of the substitute specification.

Appellants respectfully point out that "can be" is not "might be." As used in the subject specification, "can be" is an affirmative statement of possession of a capacity: the ligand **can be** used to identify the binding site on the DNA/RNA region. On the other hand, "might be" is used to indicate a degree of possibility or probability that is weaker than "may." See enclosed definitions of "can," "may" and "might" in The American Heritage Dictionary (2nd College Ed. 1991), Houghton Mifflin, Co., Boston, MA, in section IX, the Evidence Appendix. Further, Appellants note that the Examiner has not cited any authority for her position that "can be" is equivalent to "might be."

Finally, Appellants wish to point out the literal support for claims 4-8 which depend from claim 2. Claim 4 specifies that the nucleic acid ligand used in the method of claim 2 is obtained via the SELEX method. Literal support for the SELEX method can be found in the substitute specification at page 7, line 25 to page 9, line 27; and page 19, line 27 to page 21, line 1. Claims 5-8 are directed to the method as applied to the identification of transcriptional binding sites, the identification of binding sites relevant to translation and the identification of binding sites relevant to replication. Appellants direct the Examiner's attention to the literal support that can be found at page 41, lines 13-22.

In view of the foregoing, Appellants respectfully submit that *prima facie* lack of written description for claims 2 and 4-8 has not been established. However, Appellants submit that even if *prima facie* lack of written description had been established, it is rebutted by experimental evidence of written support.

One experiment relates to T4 DNA polymerase or gp43, which is discussed briefly above, and at length in the specification (see pages 49-52 and Example 1). The gp43 protein binds to the mRNA translational operator. As mentioned above, it was already known that the minimal size of the gp43 operator on the mRNA is about 36 nucleotides and has a hairpin loop structure. SELEX was conducted using candidate sequences that were nearly identical to the wild-type operator except for the loop region which was completely randomized (page 50, lines 11-14). This experiment determined how the SELEX selected ligands compared to the wild-type sequence. Three independent SELEX procedures gave similar consensus sequences for the 8 base loop sequence. Within that consensus sequence, there was some bias for the wild-type loop sequence in two of the SELEX experiments (page 51, lines 14-20). The selected ligands all acted as inhibitors of gp43 polymerase activity on the wild-type operator sequence (page 52, lines 11-13).

In short, the SELEX process produced gp43 ligands that exhibited homology with or identity to the wild-type binding site (translational operator) on the mRNA to which gp43 normally binds. Thus, the ligand to gp43 that inhibited its binding to the mRNA translational operator, could have, if the information had not already been known, provided a great deal of information about the identity and sequence of the wild-type translational operator. The fact that the wild-type sequence was already known takes nothing away from the fact that the SELEX-generated ligands to gp43 that inhibited gp43's binding to its target mRNA, were useful in providing information about the sequence of the wild-type operator. The known wild-type sequence served as a control or affirmation that the SELEX ligands had homology or identity to the wild-type sequence.

Additionally, in Example 3, RNA ligands to bacteriophage R17 coat protein were identified. R17 coat protein represses R17 replicase RNA (Carey *et al.* (1983) Biochem. 22:2601). It was found that the "winning RNA motif," i.e., the ligand with the highest affinity for the coat protein, bore a direct relationship to the coat binding site on the

natural R17 genome identified earlier though site-directed mutagenesis and binding studies (page 62, lines 28-29 of the substitute specification). Thus, in this example, a nucleic acid ligand to a binding protein that has no catalytic activity and acts only as a repressor, was found to be directly related (have homology) to the wild-type binding site found in the natural genome. Again, the fact that the wild-type sequence for the coat protein binding site on the R17 genome was already known, takes nothing away from the fact that the SELEX-generated ligands to the coat binding protein that inhibited the binding protein's binding to its target RNA, were useful in providing information about the sequence of the wild-type operator. The prior knowledge of the wild-type binding site on the R17 genome merely served as a control, affirming that selected ligands did in fact have homology or identity to the wild-type sequence.

Further, in Example 13, nucleic acid ligands to HIV-1 rev protein were identified. The rev protein binds to the rev response element (RRE) in an HIV-1 mRNA. The RRE is reported to assume a complex configuration in its recognition of rev, and the rev-RRE interaction is believed to mediate export of HIV structural messenger RNAs from the nucleus to the cytoplasm (Olsen *et al.* (1990) Science 247:845). The SELEX method yielded 53 isolates which were analyzed in a secondary structure prediction program, along with the wild type RRE. It was found that nucleic acid ligands segregated into 3 different structural motifs. The folded sequences of representatives of each motif are shown in Figure 23 along with the folded sequence of the wild-type RRE. One domain of the wild-type RRE closely resembled Motif II. Thus, the structure of nucleic acid ligands can be and was used to elucidate the structure of the naturally-occurring mRNA that binds to the rev protein. Specifically, on page 79, lines 13-17 of the substitute specification, it is reported that the conservation of certain nucleotides and structures is common to Motifs I and II as well as to wild-type RRE. When a base pair substitution occurred in conserved nucleotides, the resulting ligand had a reduced affinity compared to most other Motif I sequences. This information provided identification of the binding site structure of RRE critical for binding to the rev protein.

Further rebutled evidence can be found in Example 12 (identification of translational binding site, pseudoknot, in rRNA for binding of 305 ribosomal protein S1 of E. coli); and Example 2 (identification of replication binding site in relation to HIV-1

reverse transcriptase binding to a pseudoknot).

In view of the foregoing experimental evidence, it is respectfully submitted that Appellants have provided abundant experimental evidence of written description in rebuttal of any *prima facie* case of lack of written description of claims 2 and 4-8.

B. The Rejection of Claims 2, 3[sic] and 5-8 under 35 USC § 102(b)

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 102(b)

35 USC §102(b) provides:

> A person shall be entitled to a patent unless . . .
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States .
> . . .

In order for a reference to anticipate, it must contain all the essential elements of the claimed invention (*Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81, 90 (Fed. Cir. 1986)).

2. The Rejection of Claims 2, 3[sic] and 5-8 under 35 USC § 102(b) is improper

Claims 2, 3[sic] and 5-8 stand rejected under 35 USC §102(b) over Giordano *et al.*, U.S. Pat. No. 5,859,227 (the '227 patent) and claims 2, 3[sic], 5, 6 and 8 stand rejected under 35 USC §102(b) over Weissman *et al.*, U.S. Pat. No. 5,861,246 (the '246 patent).

Appellants respectfully submit that this rejection is procedurally improper. The Examiner advised in the final Office Action that the effective filing date for the subject claims is February 13, 2002 [sic, January 22, 2002], the filing date of the Preliminary Amendment. (Office Action, page 2, under heading "Application status"). The filing date of the subject application, however, is October 18, 2001. If the claims added on January 22, 2002, are not, as the Examiner contends, adequately described in the specification, then they are not entitled to any effective date. Moreover, claims added by

preliminary amendment after the filing date of the application may not be accorded the filing date of the preliminary amendment. Rather, if any effective date is to be accorded to the claims, it must be the filing date of the subject application or its predecessors. Since the subject application claims priority through a chain of continuation applications back to a predecessor application (U.S. Application Serial No. 07/714,131) filed June 10, 1991, any effective date accorded the claims must be June 10, 1991. Such effective date would, of course, preclude the possibility of prior art rejections over the '227 and '246 patents.

The Appellants therefore respectfully submit that the prior art rejections of the pending claims are inconsistent with the Examiner's position that the claims are not adequately described under Section 112, first paragraph.

Nonetheless, Appellants address the substance of each of the prior art rejections. As an initial matter, Appellants respectfully point out that claim 3 has been cancelled.

i. Claims 2, 3[sic] and 5-8.

Claims 2 and 5-8 stand rejected under Section 102(b) over U.S. Pat. No. 5,859,227. The '227 patent describes a method for determining RNA binding sites for RNA binding proteins. The method comprises mixing the binding protein with the RNA molecules (preferably untranslated regions) in a universal, optimized binding solution, and detecting interactions between the binding proteins and the RNA molecules. Detection can be via labels on the binding protein or RNA molecule. Once interaction is detected, the sequence of the RNA molecule is examined for known binding motifs or structural motifs which may indicate the location of the binding site. The Examiner refers specifically to col. 11, lines 61-64 and col. 11, line 64 to col. 12, line 1, which are reproduced below:

> Another preferred mode for the disclosed method, which is a binding site identification mode, involves screening RNA molecules for interactions between the RNA molecules and RNA binding proteins. The specific binding sites in the RNA molecules can then be identified by assaying interactions between RNA binding proteins and RNA molecules representing subfragments of RNA molecules identified as interacting with RNA binding proteins.

The Examiner argues that the above passage teaches that the RNA molecule is mixed with an RNA binding protein and an RNA binding region subfragment, and the binding protein binding to RNA binding region subfragment is determined, whereby the nucleotide sequence of the binding site is determined. (Office Action, page 6, subsection 7. paragraph 2). Appellants respectfully submit that the cited passage does not teach a competition assay between the RNA molecule and the subfragments for the binding to the RNA binding protein. Rather, it appears that the passage teaches that subfragments are assayed for binding to RNA binding proteins.

In addition, Appellants point out that the subfragments are derived directly from the RNA molecules, and as such are necessarily identical over their length to the RNA molecules from which they are derived. They are not nucleic acid ligands as prepared according to the SELEX method as is described in the subject application.

Thus, the '227 patent does not meet the anticipation standard of teaching all of the essential elements of the claimed invention (*Hybritech*, *supra* at 231 USPQ 90).

For the foregoing reasons, it is submitted that the '227 patent does not anticipate any of the subject claims.

ii. Claims 2, 3[sic] and 5-8.

Claims 2, 5, 6 and 8 stand rejected under Section 102(b) over U.S. 5,861,246. The '246 patent describes a multiplex selection technique in which a nuclear extract containing a number of transcription factors is mixed with randomized oligonucleotides. Complexes of transcription factor and oligos are separated from unbound material, and selected oligos are amplified. This procedure can be repeated. Ultimately the selected and amplified oligos are cloned to generate a library of "binding sites" (col. 8, lines 15-26). Members of this library can be used to identify transcription factors. Several factors, including OctT3, were known to complex with wt-Oct sequence. An experiment was conducted to determine whether wt-Oct was the highest affinity "binding site" in the library for OctT3. It was found that the BS08 sequence from the binding site library was the highest affinity sequence for the OctT3. The experiment involved competing OctT3-wt-Oct complex with other probes in the TP2-4 binding site library. The Examiner argues that this experiment anticipates subject claim 2. (Office Action, page 7, paragraph

1).

Appellants respectfully point out that subject claim 2 is directed to a method of identifying the DNA/RNA binding site in a DNA/RNA region by competing a nucleic acid ligand to the binding protein with the DNA/RNA region. The '246 patent describes only the identification of the probe from the library with the highest affinity to the OctT3 protein. The probe of the highest affinity from the library is not necessarily the wild-type binding site to which the OctT3 binds. In other words, the nucleic acid ligand of the subject invention is used to identify or determine the sequence of the actual binding site within a region of DNA/RNA. In the '246 patent, the goal of the procedure is to identify the probe of highest binding affinity. Thus, the '246 patent does not meet the anticipation standard of teaching all of the essential elements of the claimed invention (*Hybritech, supra* at 231 USPQ 90).

For the foregoing reasons, it is submitted that the '246 patent does not anticipate any of the subject claims. Appellants respectfully requests therefore that the Section 102(b) rejection over the '246 patent be withdrawn.

C. The Rejection of Claim 4 under 35 USC §§ 102(b)/103

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 103

The Examiner bears the burden of establishing a *prima facie* case of obviousness under 35 USC § 103. In determining obviousness, one must focus on Applicant's invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 USPQ2d 1241,1246 (Fed. Cir. 1991). The primary inquiry is:

> whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success . . . Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

In re Dow Chemical, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

Where the prior art teaches away from the combination of elements recited in the claimed invention, the reference cannot be said to support *prima facie* obviousness (*Mentor H/S, Inc. et al. v. Medical Device Alliance, Inc. et al.*, 244 F.3d 1365, 1377, 58

USPQ2d 1321, 1326-27 (Fed. Cir. 2001).

2. The Rejection of Claim 4 under 35 USC §§ 102(b)/103 is improper

Claim 4 stands rejected under Sections 102(b)/103 over Weissman *et al.*, U.S. Pat. 5,861,246 (the '246 patent). The Examiner contends that the SELEX method, or something similar to it, is set forth at col. 4, lines 36-50 of the '246 patent, and that therefore the skilled artisan would have been motivated to use same in obtaining a nucleic acid ligand to a DNA/RNA binding protein. (Office Action, page 8).

Initially, Appellants point out that, as discussed above in relation to the Section 102(b) rejections, it is procedurally improper for the Examiner to make a prior art rejection when she has maintained that the pending claims are not supported by adequate written description. Claims added by amendment after the filing date of the application cannot be given as an effective date, the filing date of the amendment. If they are to be given any effective date, it must be that of the filing date of the pending application or its predecessors. Since the subject application is identical to a series of predecessors going back to USSN 07/714,131, filed on June 10, 1991, then any effective date of the subject claims must be June 10, 1991. In that case, the '246 patent is not proper prior art.

Nonetheless, Appellants address the substance of the subject rejection. Appellants respectfully submit that even if the SELEX method is taught in the '246 patent, claim 4 is novel and non-obvious because claim 2, from which claim 4 depends, is novel and non-obvious. As discussed above, the '246 patent does not teach all of the elements of claim 2 because it teaches only finding the probe of highest affinity in a "binding site" library. It does not teach identifying the actual binding site within an RNA/DNA region for a binding protein. Claim 2 is non-obvious over the '246 patent because the method of the '246 patent is a "multiplex selection technique" which identifies numerous (hundreds or thousands?) of synthetic probes that bind to numerous (hundreds or thousands?) of factors in a cell or nuclear extract. The '246 patent does not direct the skilled artisan to identification of the actual binding site for a DNA/RNA binding protein within a region of DNA or RNA. In fact, the '246 patent teaches away from the subject claimed method:

> The technical beauty of the MuST procedure is essentially that by using a complex mixture of targets in the selection steps one can, in a relatively small number of selection cycles, obtain a mixture that is predominantly made up of specific probes containing optimal sequences. By starting with two complex mixtures (i.e., both probes and targets), one can obtain a high ratio of specifically retained material to non-specific background in the early cycles, without working with concentrations of probe or target such that large amounts of more weakly binding material is retained. (col. 5, lines 11-20).

As discussed above, a prior art reference that teaches away from the combination of elements recited in a claimed invention, does not support *prima facie* obviousness of that claim (*Mentor H/S, Inc. et al., supra* at 58 USPQ2d at 1326-27). Therefore, Appellants respectfully request that in view of the foregoing arguments, the Sections 102(b)/103 rejections be withdrawn.

VIII. CLAIMS APPENDIX

1. (Canceled).

2. (Previously presented) A method for identifying a nucleic acid binding protein's binding site on a region of a DNA or RNA comprising:

a) providing a nucleic acid ligand to the nucleic acid binding protein;

b) adding said nucleic acid ligand to said nucleic acid binding protein and said DNA or RNA region; and

c) determining whether said added nucleic acid ligand inhibits said protein from binding to said RNA or DNA region, whereby the sequence or structure of said inhibitory nucleic acid ligand assists in the identification of the binding site in the DNA or RNA region.

3. (Canceled).

4. (Previously presented) The method of claim 2 wherein said nucleic acid ligand is provided by the method comprising the steps of:

a) contacting a candidate mixture of nucleic acids each of which have a randomized

sequence with the binding protein, whereby nucleic acids having an increased affinity to the protein relative to the candidate mixture may be partitioned from the remainder of the candidate mixture;

b) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture; and

c) amplifying the increased affinity nucleic acids to yield a ligand-enriched mixture of nucleic acids, whereby a nucleic acid ligand of the protein may be identified.

5. (Previously presented) The method of claim 2 wherein the DNA or RNA region is contains a site selected from the group consisting of a promoter, an origin of replication, a ribosomal binding site and a tRNA binding site.

6. (Previously presented) The method of claim 2 wherein the protein regulates transcription.

7. (Previously presented) The method of claim 2 wherein the protein regulates translation.

8. (Previously presented) The method of claim 2 wherein the protein is selected from the group consisting of transcriptional activators, transcriptional repressors, transcription complexes at promoter sites, replication accessory proteins, DNA polymerases, RNA polymerases and translational repressors.

IX. EVIDENCE APPENDIX

Enclosed please find copies of the following references relied upon by the Examiner as to the grounds of rejection to be reviewed upon appeal.

- Giordano *et al.*, U.S. Pat. No. 5,859,227
- Weissman *et al.*, U.S. Pat. No. 5,861,246

Also enclosed please find a copy of the following reference relied upon by the Applicant

as to the grounds of rejection to be reviewed upon appeal.

- The American Heritage Dictionary (2d College Ed. 1991), Houghton Mifflin Co., Boston, MA, pp. 232, 774, 795

X. CLOSING REMARKS

For the foregoing reasons, Appellants submit that the pending claims 2 and 4-8 are adequately described by the specification under 35 USC §112, first paragraph. Appellants also submit that the 35 §§102(b) and 103 rejections are improper and inconsistent regardless of whether or not the subject claims are adequately described. If the subject claims do have adequate written description in the specification, then they are entitled to an effective date of June 10, 1991, and the cited art has 35 USC §§102(e) and 102(b) dates after said effective date. If the subject claims are not adequately described, then they are not entitled to any effective date, and in particular are not entitled to an effective date of the post-filing preliminary amendment filing date; they cannot therefore be the subject of a prior art rejection.

Enclosed is a check for $450.00 for the Appeal Brief fee and the one month extension of time. It is believed that no other fees are due with this Appeal Brief. If this is in error, please charge any necessary fees to Deposit Account No. 19-5117.

Respectfully submitted,

Date: October 12, 2004

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Second College Edition

The American Heritage Dictionary

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image of an object is focused and recorded on a photosensitive film or plate. **2.** The part of a television transmitting apparatus that receives the primary image on a light-sensitive cathode tube and transforms it into electrical impulses. **3.** A camera obscura. **4.** *pl.* **-er·ae** (-ə-rē). A judge's private chamber. [LLat., room. —see CHAMBER.]

cam·er·al (kăm'ər-əl) *adj.* **1.** Pertaining to a judge's chamber and to the judicial affairs that take place there. **2.** Pertaining to public finance and state business or to a council that manages such matters. [Med. Lat. *cameralis* < *camera,* office < LLat., room. —see CHAMBER.]

camera lu·ci·da (lōō'sĭ-də) *n.* An optical device that projects a virtual image of an object onto a plane surface, esp. for tracing. [NLat., light chamber.]

cam·er·a·man (kăm'ər-ə-măn', kăm'rə-) *n.* A person who operates a motion picture or television camera.

camera ob·scu·ra (əb-skyŏŏr'ə) *n.* A darkened chamber in which the real image of an object is received through a small opening or lens and focused in natural color onto a facing surface. [NLat., dark chamber.]

cam·er·lin·go (kăm'ər-lĭng'gō) also **cam·er·len·go** (-lĕng'-gō) *n., pl.* **-gos.** *Rom. Cath. Ch.* The cardinal who manages the pope's secular affairs. [Ital. *camarlingo.*]

cam·i·on (kăm'ē-ən, kăm-yŏn') *n.* **1.** A low, sturdy wagon. **2. a.** A truck. **b.** A bus. [Fr. < OFr. *chamion.*]

ca·mi·sa (kə-mē'sə) *n. Southwestern U.S.* A shirt or chemise. [Sp. < LLat. *camisia,* shirt.]

cam·i·sa·do (kăm'ĭ-sä'dō, -sä'-) *n., pl.* **-dos.** *Archaic.* A surprise attack by night. [Prob. < Sp. *encamisado,* shirted (so called because the attackers wore white shirts over their armor for identification) < *camisa,* shirt. —see CAMISA.]

ca·mise (kə-mēz', -mēs') *n.* A loose shirt, shift, or tunic. [Ar. *qamīs* < LLat. *camisia,* shirt.]

cam·i·sole (kăm'ĭ-sōl') *n.* **1.** A woman's sleeveless undergarment. **2.** A short negligee. [Fr. < OProv. *camisolla,* dim. of *camisa,* shirt < LLat. *camisia.*]

Cam·lan (kăm'lən) *n.* The legendary battlefield where King Arthur was mortally wounded.

cam·let (kăm'lĭt) *n.* **1.** A rich cloth of Oriental origin, supposed originally to have been made of camel's hair and silk and later made of goat's hair and silk or other combinations. **2.** A garment made from camlet. [ME *chamelet* < OFr. *chamelot* < Ar. *ḥamlat.*]

cam·o·mile (kăm'ə-mīl') *n.* Variant of **chamomile.**

Ca·mor·ra (kə-môr'ə, -mŏr'ə) *n.* **1.** A Neapolitan secret society organized about 1820, notorious for practicing violence and blackmail. **2.** An unscrupulous, clandestine group. [Ital., perh. < *camorra,* a kind of smock, said to have been worn by members of the society.]

cam·ou·flage (kăm'ə-fläzh', -fläj') *n.* **1.** The method or result of concealing personnel or materiel from an enemy by making them appear to be part of the natural surroundings. **2.** A means of concealment; dissimulation. —*tr. & intr.v.* **-flaged, -flag·ing, -flag·es.** To conceal by or use camouflage. [Fr. < *camoufler,* to disguise < Ital. *camuffare.*] **—cam'ou·flag'er** *n.*

campanile
Campanile of Florence Cathedral designed by Giotto

camper

camp¹ (kămp) *n.* **1. a.** A place where a group of people, such as soldiers, are temporarily lodged in tents, huts, or other makeshift shelters. **b.** The shelters in such a place. **c.** The persons using such shelters. **2.** A place consisting of more or less permanent cabins or other shelters, used for vacationing or other recreational purposes. **3.** Military service; army life: *recruits getting used to the routine in camp.* **4.** A group of persons, parties, or states favorable to a common cause, doctrine, or political system: *the socialist camp.* —*v.* **camped, camp·ing, camps.** —*tr.* To shelter or lodge in a camp; encamp. —*intr.* **1.** To make or set up a camp. **2.** To live in or as if in a camp; settle: *camped in the apartment until the furniture arrived.* [OFr. < Lat. *campus,* field.]

camp² (kămp) *n.* **1. a.** An affectation or appreciation of manners and tastes commonly thought to be outlandish, vulgar, or banal. **b.** Behavior exhibiting such affectation or appreciation. **2.** Banality or artificiality when appreciated for its humor. —*adj.* Having the qualities or style of camp. —*intr.v.* **camped, camp·ing, camps.** To act in an outlandish, vulgar, or banal manner. [Orig. unknown.] **—camp'y** *adj.*

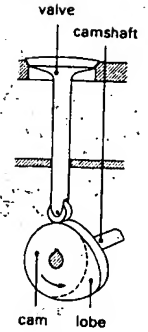
cam·paign (kăm-pān') *n.* **1.** A series of military operations undertaken to achieve a specific objective within a given area. **2.** An operation undertaken, as by means of propaganda, to attain some political, social, or commercial goal. —*intr.v.* **-paigned, -paign·ing, -paigns.** To engage in a campaign. [Fr. *campagne* < OFr., battlefield < OItal. *campagna* < LLat. *campania,* open country < *campus,* field.] **—cam·paign'er** *n.*

cam·pa·ni·le (kăm'pə-nē'lē) *n., pl.* **-les** (-lēz) or **-li** (-lē). A bell tower, esp. one near but not attached to a church. [Ital. < *campana,* bell < LLat.]

cam·pa·nol·o·gy (kăm'pə-nŏl'ə-jē) *n.* The art or study of bell casting and ringing. [LLat. *campana,* bell + **-LOGY.**] **—cam'pa·nol'o·gist** *n.*

cam·pan·u·la (kăm-păn'yə-lə) *n.* Any of various plants of the genus *Campanula,* which includes the bellflowers. [NLat. *Campanula,* genus name, dim. of LLat. *campana,* bell.]

cam·pan·u·late (kăm-păn'yə-lĭt, -lāt') *adj. Bot.* Bell-shaped. [NLat. *campanula,* dim. of LLat. *campana,* bell + **-ATE¹.**]



camshaft

camp·er (kăm'pər) *n.* **1.** One that camps. **2. a.** A compact, vanlike vehicle resembling an automobile-and-trailer combination, designed to serve as a dwelling and used for camping or on long motor trips. **b.** A portable shelter resembling the top part of a trailer, made to be mounted on a pickup truck to form such a vehicle.

cam·pes·tral (kăm-pĕs'trəl) *adj.* Of, pertaining to, or growing in uncultivated land or open fields. [Lat. *campester,* of a field < *campus,* field.]

cam·pes·tri·an (kăm-pĕs'trē-ən) *adj.* Pertaining to the northern Great Plains. [< Lat. *campestria,* a plain < *campus,* field.]

camp·fire (kămp'fīr') *n.* **1.** An outdoor fire in a camp, used for warmth or cooking. **2.** A meeting held around a campfire.

camp fire girl *n.* A member of the Camp Fire Girls, an organization for girls from 7 through 18 that strives to instill good values and character and develop practical skills.

camp follower *n.* **1.** A civilian who follows an army from place to place to sell goods or services. **2.** One who follows but does not belong to a main body or group.

camp·ground (kămp'ground') *n.* An area used for setting up a camp or holding a camp meeting.

cam·phene (kăm'fēn') *n.* A colorless crystalline compound, $C_{10}H_{16}$, used in the manufacture of synthetic camphor and insecticides. [CAMPH(OR) + **-ENE.**]

cam·phor (kăm'fər) *n.* A volatile crystalline compound, $C_{10}H_{16}O$, obtained from camphor tree wood or synthesized and used as an insect repellent, in the manufacture of film, plastics, lacquers, and explosives, and medicinally as a stimulant, expectorant, and diaphoretic. [ME *caumfre* < OFr. *camphre* < Med. Lat. *camphora* < Ar. *kāfūr.*] **—cam·phor'ic** (-fôr'ĭk, -fŏr'-) *adj.*

cam·phor·ate (kăm'fə-rāt') *tr.v.* **-at·ed, -at·ing, -ates.** To treat or impregnate with camphor.

camphor ice *n.* A skin ointment consisting of camphor, white wax, spermaceti, and castor oil.

camphor oil *n.* The oil obtained from the wood of the camphor tree.

camphor tree *n.* An evergreen tree, *Cinnamomum camphora,* native to eastern Asia, having aromatic wood that is a source of camphor.

cam·pi·on (kăm'pē-ən) *n.* Any of various plants of the genus *Lychnis* or related genera, having red, pink, or white flowers. [Orig. unknown.]

camp meeting *n.* An evangelistic gathering held in a tent or outdoors and often lasting a number of days.

cam·po (kăm'pō, kăm'-) *n., pl.* **-pos.** A large, grassy plain in South America, with occasional bushes and small trees. [Am. Sp. < Sp., field < Lat. *campus.*]

camp·o·ree (kăm'pə-rē') *n.* An assembly or gathering of Boy Scouts on a local or district level. [CAMP + (JAMB)OREE.]

camp robber *n.* The Canada jay.

camp·site (kămp'sīt') *n.* An area suitable or used for camping.

camp·stool (kămp'stōōl') *n.* A light folding stool.

cam·pus (kăm'pəs) *n., pl.* **-pus·es.** **1.** The grounds of a school, college, or university. **2.** A field in ancient Rome used for various events, such as military exercises. [Lat., field.]

cam·py·lot·ro·pous (kăm'pə-lŏt'rə-pəs) *adj. Bot.* Having the ovule partially inverted and curved. [Gk. *kampulos,* curved + **-TROPOUS.**]

cam·shaft (kăm'shăft') *n.* An engine shaft fitted with a cam or cams.

can¹ (kăn; kən *when unstressed*) *aux.v.* Past tense **could** (kŏŏd). **1.** Used to indicate: **a.** Physical or mental ability: *I can meet you today.* **b.** Possession of a specified power, right, or privilege: *The President can veto congressional bills.* **c.** Possession of a specified capacity or skill: *He can tune the harpsichord as well as play it.* **2.** Used to indicate possibility or probability: *I wonder if she can still be alive.* **3.** Used to request or grant permission: *Can I be excused? No, you cannot.* [ME < OE, first and third person pr. indicative of *cunnan,* to know how.]

Usage: Generations of grammarians and schoolteachers have insisted that *can* should be used only to express the capacity to do something, while *may* must be used to indicate permission. Technically, correct usage therefore requires: *The boss said that anyone who wants an extra day off may* (not *can*) *have one. May* (not *can*) *I have an extra blanket?* In speech, however, *can* is used to express permission by most speakers, and the "permission" use of *can* is even more frequent in British English. The negative contraction *can't* is frequently used in coaxing and wheedling questions like *Can't I have the car tonight?* Many members of the Usage Panel feel also that the alternative contraction *mayn't* is awkward and unnatural.

can² (kăn) *n.* **1.** A usually cylindrical metal container. **2. a.** An airtight container, usually made of tin-coated iron, in which foods or beverages are preserved. **b.** The contents of such a container. **3.** *Slang.* A jail or prison. **4.** *Slang.* A toilet or rest room. **5.** *Slang.* The buttocks. —*tr.v.* **canned, can·ning, cans. 1.** To seal in a can or jar for future use;

preserve. **2.** *Slang.* To make a record
ence's applause. **3.** *Slang.* **a.** To dismiss
school. **b.** To quit or dispense with:
canne, a water container < OE.] **—can**

Can·a·da balsam (kăn'ə-də) *n.* **1.** The
cous, yellowish, transparent resin obta
fir and used as a mounting cement fo
mens.

Canada goose *n.* A common wild goos
of North America, having grayish plu
and head, and a white face patch.

Canada jay *n.* A bird, *Perisoreus ca*
American conifer forests, having gray p
capped head.

Canada thistle *n.* A weedy plant, *Cirsiu*
Eurasia, having prickly leaves and clust
ers.

Ca·na·di·an bacon (kə-nā'dē-ən) *n.* C
from the loin of a pig.

Canadian French *n.* The language of
dians.

ca·naille (kə-nī', -nāl') *n.* The masses c
rabble; riffraff. [Fr. < Ital. *canaglia* < *ca*
nis.]

ca·nal (kə-năl') *n.* **1.** A manmade water
improved river used for irrigation, sh
2. *Anat.* A tube or duct. **3.** *Astron.* One
markings resembling straight lines on th
—*tr.v.* **-naled, -nal·ing, -nals** or **-nale**
1. To dig an artificial waterway through.
a canal or canals. [Partly < Fr., channel,
tube, both < Lat. *canalis,* tube, channel.]

can·a·lic·u·late (kăn'ə-lĭk'yə-lĭt, -lāt') *adj.*
or channels. [Lat. *canaliculatus* < *canaliculu*
channel.]

can·a·lic·u·lus (kăn'ə-lĭk'yə-ləs) *n., pl.* -
bodily channel, as a tear duct. [Lat., dim
duit.] **—can·a·lic'u·lar** (-lər) *adj.*

can·a·li·za·tion (kăn'ə-lĭ-zā'shən) *n.* **1.** Th
stance of canalizing. **2.** A system of canals

can·a·lize (kăn'ə-līz') *tr.v.* **-lized, -liz·ing,**
nish with, build, or convert into a canal
channel into a particular direction; provi

canal rays *pl.n.* Positively charged ions for
electrical discharge and attracted to the ca
charge tube. Not in current technical use
Kanalstrahl (from the fissures in the cathod
the ions pass).]

can·a·pé (kăn'ə-pā', -pē) *n.* A cracker or sm
bread or toast spread with cheese, meat, or r
as an appetizer. [Fr. < *canapé,* couch < Med.
mosquito net. —see CANOPY.]

ca·nard (kə-närd') *n.* An unfounded or fal
misleading story. [Fr., prob. < the phrase *ven*
moitié, to half-sell a duck, to swindle.]

ca·nar·y (kə-nâr'ē) *n., pl.* **-ies. 1.** A songbi
naria, native to the Canary Islands, that is g
low and has long been bred as a cage bird
informer; stool pigeon. **3.** A sweet white w
Madeira, from the Canary Islands. **4.** A livel
court dance. **5.** A light to moderate or vivi
canari < OSp. *canario* < (*Islas*) *Canarias,* Can
LLat. *Canariae* (*Insulae*), (islands) of dogs
dog.]

canary grass *n.* A grass, *Phalaris canariensis,*
rope, having straw-colored seeds used to feed

ca·nas·ta (kə-năs'tə) *n.* A card game for two
related to rummy and requiring two decks of
canasto, basket < Lat. *canistrum.* —see CANIST

can-can (kăn'kăn') *n.* An exuberant dance,
France, performed by women and marked by
[Fr.]

can·cel (kăn'səl) *v.* **-celed, -cel·ing, -cels** also
-elled, -el·ling, -els. —*tr.* **1.** To cross out with lines or
ings. **2.** To annul or invalidate: *cancel an invi*
mark or perforate (a postage stamp, for example
that it may not be used again. **4.** To equalize
for; offset. **5.** *Math.* **a.** To remove a common
the numerator and denominator of a fractional
b. To remove a common factor or term from bo
of an equation or inequality. **6.** *Printing.* To om
—*intr.* To balance or neutralize one another: *tw*
canceled out. —*n.* **1. a.** The omission or deletion
printed matter. **b.** The matter omitted or delete
placement. **2.** A part of a book used as a subst
original part of the book. [ME < Norman Fr. *can*
cancellare, to cross out < *cancelli,* lattice, dim.
lattice.] **—can'cel·a·ble** *adj.* **—can'cel·er** *n.*

can·cel·a·tion (kăn'sə-lā'shən) *n.* Variant of **ca**

can·cel·late (kăn-sĕl'āt, kăn'sə-lāt') also **can**
(-lā'tĭd). *adj. Anat.* Cancellous. [Lat. *cancellatus,*
cancellare, to make like a lattice. —see CANCEL.]

can·cel·la·tion also **can·ce·la·tion** (kăn'sə-lā
1. The act of canceling. **2.** Marks or perforations
canceling. **3.** Something that has been canceled.

max·il·lar·y (māk'sə-lĕr'ē) *n., pl.* **-les.** A jaw or jawbone. **—max'il·lar'y** *adj.*

max·il·li·ped (māk-sĭl'ə-pĕd') *n. Zool.* One of the three pairs of crustacean head appendages located just posterior to the maxillae. [MAXILL(A) + -PED.]

max·il·lo·fa·cial (māk-sĭl'ō-fā'shəl) *adj.* Pertaining to or involving the maxilla and the face. [MAXILL(A) + FACIAL.]

max·im (māk'sĭm) *n.* A concise formulation of a fundamental principle or rule of conduct; saying. [ME *maxime* < OFr. < Med. Lat. *maxima* < Lat. *maximus*, greatest < *magnus*, great.]

max·i·ma (māk'sə-mə) *n.* A plural of **maximum.**

max·i·mal (māk'sə-məl) *adj.* **1.** Of, pertaining to, or consisting of a maximum. **2.** Being the greatest or highest possible. **3.** *Math.* Designating the maximal of an ordered set. *—n. Math.* An element in an ordered set that is followed by no other. **—max'i·mal·ly** *adv.*

max·i·mal·ist (māk'sə-mə-list) *n.* One who advocates direct revolutionary action to secure social and political gains. [Fr. *maximaliste*, prob. < E. *maximal.*]

max·i·mize (māk'sə-mīz') *tr.v.* **-mized, -miz·ing, -miz·es. 1.** To increase or make as great as possible: *"the ideal of maximizing opportunity through the equalizing of educational opportunity"* (Robert J. Havighurst). **2.** To assign the highest possible importance to. **3.** *Math.* To find a maximum value of (a function). **—max'i·mi·za'tion** *n.* **—max'i·miz'er** *n.*

max·i·mum (māk'sə-məm) *n., pl.* **-mums** or **-ma** (-mə). **1. a.** The greatest possible quantity, degree, or number. **b.** The time or period during which the highest point or degree is attained. **2.** An upper limit stipulated by law or other authority. **3.** *Astron.* **a.** The moment when a variable star is most brilliant. **b.** The magnitude of the star at such a moment. **4.** *Math.* **a.** The value of a function that is not exceeded by neighboring values. **b.** The greatest value assumed by a function within some subset of its domain of definition. **c.** The largest number in a set. *—adj.* **1.** Having or being the greatest quantity or the highest degree that has been or can be attained: *maximum temperature.* **2.** Of, pertaining to, or making up a maximum: *a maximum number in a series.* [< Lat., neuter of *maximus*, greatest. —see MAXIM.]

ma·xixe (mə-shēsh', -shē'shə) *n.* A Brazilian dance similar to the two-step. [Port. (Brazil).]

max·well (māks'wĕl', -wəl) *n.* A unit of magnetic flux in the centimeter-gram-second electromagnetic system, equal to the flux perpendicularly intersecting an area of one square centimeter in a region where the magnetic induction is one gauss. [After James *Maxwell* (1831–1879).]

may (mā) *aux.v.* Past **might** (mīt), present **may** for singular and plural. **1.** To be allowed or permitted to: *May I take a swim? You may.* **2.** Used to indicate a certain measure of likelihood or possibility: *It may rain this afternoon.* **3.** To be obliged; must. Used in statutes, deeds, and other legal documents. **4.** Used to express a desire or fervent wish: *Long may he live!* **5.** Used to express contingency, purpose, or result, in clauses introduced by *that* or *so that: expressing ideas so that the average man may understand.* —See Usage note at **can.** [ME, to be able < OE *mæg*, 1st and 3rd person singular indicative of *magan*, to be strong, be able.]

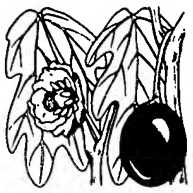
May (mā) *n.* **1.** The fifth month of the year according to the Gregorian calendar. See table at **calendar. 2.** The springtime of life; youth. **3.** The celebration of May Day. **4. may.** *Chiefly Brit.* The blossoms of the hawthorn. [ME < OFr. *Mai* < Lat. *Maius* < *Maia*, an Italic goddess.]

ma·ya (mä'yə) *n. Hinduism.* **1.** The origin of the world. **2.** The illusory appearance of the world. [Skt. *māyā.*]

Ma·ya (mä'yə) *n., pl.* **Maya** or **-yas. 1.** A member of a race of Indians in southern Mexico and Central America whose civilization reached its height around A.D. 1000. **2.** The Mayan language of the Maya. [Sp.] **—Ma'ya** *adj.*

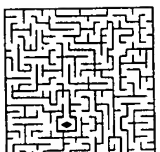
Ma·yan (mä'yən) *adj.* Of or pertaining to the Mayas, their culture, their language or the language group to which it belongs. *—n.* **1.** A Maya. **2.** A linguistic stock of Central America that includes Maya and Yucatec.

May apple *n.* **1.** A plant, *Podophyllum peltatum*, of eastern North America, having a single, nodding white flower and oval yellow fruit. Although the pulp of the ripe fruit is edible, the roots, leaves, and seeds of this plant are poisonous. **2.** The fruit of the May apple.



May apple

Maypole



maze

may·be (mā'bē) *adv.* Perhaps; possibly.

May beetle *n.* The June beetle.

may·day (mā'dā') *n.* An international radio-telephone signal word used by aircraft and ships in distress. [Alteration of Fr. *m'aidez*, help me!]

May Day *n.* **1.** The first day of May, marked by the celebration of spring. **2.** May 1, regarded in a number of places as an international holiday to celebrate labor organizations.

may·est (mā'ĭst) or **mayst** (māst) *aux.v. Archaic.* Second person singular present tense of **may**[1].

may·flow·er (mā'flou'ər) *n.* **1.** Any of a wide variety of plants that bloom in May. **2.** The trailing arbutus.

may·fly (mā'flī') *n.* Any of various fragile, winged insects of the order Ephemeroptera that develop from aquatic nymphs and live in the adult stage for only a few hours.

may·hap (mā'hăp', mā-hăp') *adv.* Perhaps; perchance. [< the phrase *it may hap.*]

may·hem (mā'hĕm', mā'əm) *n.* **1.** *Law.* The offense of willfully maiming or crippling a person. **2.** The infliction of violent injury upon a person or thing; wanton destruction: *children committing mayhem in the flower beds.* **3.** A state of violent disorder or riotous confusion; havoc. [ME < AN *mahem* < OFr. *mahaignier*, to maim.]

may·ing (mā'ĭng) *n.* Often **Maying.** The gathering of spring flowers, esp. during a May festival.

may·n't (mā'ənt, mānt). May not.

may·o (mā'ō) *n.* Mayonnaise.

may·on·naise (mā'ə-nāz', mā'ə-nāz') *n.* A dressing made of beaten raw egg yolk, butter or olive oil, lemon juice or vinegar, and seasonings. [Fr.]

may·or (mā'ər, mâr) *n.* The chief magistrate of a city, town, borough, or municipal corporation. [ME *maire* < OFr. < Med. Lat. *major* < Lat., greater. —see MAJOR.] **—may'or·al** *adj.* **—may'or·ship'** *n.*

may·or·al·ty (mā'ər-əl-tē, mâr'əl-) *n., pl.* **-ties. 1.** The office of a mayor. **2.** The term of office of a mayor. [ME *mairalte* < AN < OFr. *maire*, mayor. —see MAYOR.]

may·or·ess (mā'ər-ĭs, mâr'ĭs) *n.* **1.** A woman serving as the chief magistrate of a city, town, borough, or municipal corporation. **2.** The wife of a mayor.

May·pole also **may·pole** (mā'pōl') *n.* A pole decorated with streamers that May Day celebrants hold while dancing.

may·pop (mā'pŏp') *n.* **1.** A vine, *Passiflora incarnata*, of the southeastern United States, having purple and white flowers and edible yellow fruit. **2.** The fruit of the maypop. [Alteration of *maycock* < Powhatan *mahcawq.*]

mayst (māst) *aux.v.* Variant of **mayest.**

may tree *n. Chiefly Brit.* The hawthorn.

may·weed (mā'wēd') *n.* A widespread weed, *Anthemis cotula*, having rank-smelling leaves and white flowers.

May wine *n.* **1.** A still white wine with woodruff flavoring, often containing orange or pineapple slices. **2.** A punch of champagne, claret, and Moselle or Rhine wine, flavored with woodruff. [Transl. of G. *Maiwein.*]

ma·zae·di·um (mə-zē'dē-əm) *n., pl.* **-di·a** (-dē-ə). A fruiting body of some lichens in which the spores lie freely in a powdery mass that is enclosed in a peridium. [NLat.: Gk. *maza*, lump + Lat. *aedes*, house.]

ma·zal tov (mä'zəl tōf') *interj.* Variant of **mazel tov.**

Maz·da·ism also **Maz·de·ism** (măz'də-ĭz'əm) *n.* Zoroastrianism. [< Avestan *mazda*, the good principle.]

maze (māz) *n.* **1. a.** An intricate, usually confusing, network of walled or hedged pathways; labyrinth. **b.** A physical situation in which it is easy to get lost. **c.** Any of various networks of pathways, some blind and some leading to a goal, used experimentally to investigate learning in animals. **2.** A graphic puzzle, the solution of which is an uninterrupted path through an intricate pattern of line segments from a starting point to a goal. **3.** Something made up of many confused or conflicting elements; tangle. *—tr.v.* **mazed, maz·ing, maz·es. 1.** *Chiefly Regional.* To stupefy; daze. **2.** To bewilder. [ME *mase*, maze, confusion < *masen*, to confuse < OE *āmasian*, to confound.] **—maz'y** *adj.*

ma·zel tov also **ma·zal tov** (mä'zəl tōf') *interj. Hebrew.* Congratulations. [Heb. *mazālṭob* : *mazāl*, luck + *ṭob*, good.]

ma·zer (mā'zər) *n.* A large drinking bowl or goblet made of hard wood or metal. [ME < OFr. *mazre*, of Germanic origin.]

ma·zour·ka (mə-zûr'kə, -zōōr'-) *n.* Variant of **mazurka.**

ma·zu·ma (mə-zōō'mə) *n. Slang.* Money; cash. [Yiddish *mazumen* < Heb. *mzumān*, fixed.]

ma·zur·ka also **ma·zour·ka** (mə-zûr'kə, -zōōr'-) *n.* **1.** A lively Polish dance resembling the polka, frequently adopted as a ballet form. **2.** A piece of music for a mazurka, written in 3/4 or 3/8 time with the second beat heavily accented. [Pol., accusative of *mazurek*, dim. of *mazur*, someone from Mazovia, a province of Poland.]

maz·zard (măz'ərd) *n.* A wild sweet cherry, *Prunus avium*, often used as grafting stock. [Orig. unknown.]

mbi·ra (ĕm-bĭr'ə, əm-) *n.* A thumb piano. [Of Bantu orig.]

MC (ĕm'sē') *n.* A master of ceremonies.

Mc·Car·thy·ism (mə-kär'thē-ĭz'əm) *n.* **1.** The political practice of publicizing accusations of disloyalty or subversion with insufficient regard to evidence. **2.** The use of methods of investigation and accusation regarded as unfair, in order to suppress opposition. [After Joseph R. *McCarthy* (1908–1957).] **—Mc·Car'thy·ist** *n.*

Mc·Coy (mə-koi') *n. Slang.* The authentic thing or quality; something that is not an imitation or substitute: *the real McCoy.* [After Kid *McCoy* (Norman Selby, 1873–1940), American boxer.]

Mc·In·tosh (măk'ĭn-tŏsh') *n.* A variety of red eating apple grown commercially in the northern United States. [After John *McIntosh* (fl. 1796), its first cultivator.]

Md The symbol for the element mendelevium.

M-day (ĕm'dā') *n.* Mobilization day; the day on which national mobilization for war is ordered.

me (mē) *pron.* The objective case of the first person pronoun. Used: **1.** As the direct object of a verb: *He assisted me.* **2.** As the indirect object of a verb: *They offered me a ride.* **3.** As the object of a preposition: *This letter is addressed to me.* —See Usage notes at **be** and **I.** [ME < OE *mē.*]

me·a cul·pa (mā'ə kŭl'pə) *n.* An acknowledgment of a personal error or fault. [Lat., through my fault.]

mead[1] (mēd) *n.* An alcoholic beverage made from fermented honey and water. [ME < OE *medu.*]

mead[2] (mēd) *n. Archaic.* A meadow. [ME *meade* < OE *mæd*]

mead·ow (mĕd'ō) *n.* A tract of grassland, either in its natural state or used as pasture or for growing hay. [ME *mea* < OE *mædwe* < *mæd*, meadow.] **—mead'ow·y** *adj.*

meadow beauty *n.* A plant of the genus *Rhexia*, of east North America, growing in wet ground and having showy purple flowers.

meadow fescue *n.* A grass, *Festuca eliator*, used for h

meadow hen *n.* Any of various birds of the family Rallid sp. a rail or coot.

mead·ow·land (mĕd'ō-lănd') *n.* A tract of land having characteristics of or used for a meadow.

mead·ow·lark (mĕd'ō-lärk') *n.* A bird of the genus *Sturne* with two species, *S. magna*, the eastern meadowlark, and neglecta, the western meadowlark, found in North Ame and noted for their song.

meadow mouse *n.* The field mouse.

meadow mushroom *n.* An edible mushroom, *Agar campestris*, that thrives in moist soil and is cultivated human consumption.

meadow nematode *n.* Any of various nematodes of genus *Pratylenchus* that are parasitic on the roots of pla

meadow rue *n.* Any of various plants of the genus *Tha* fam. having clusters of small white, yellowish, or purp flowers.

meadow saffron *n.* The autumn crocus.

mead·ow·sweet (mĕd'ō-swēt') *n.* Any of several plants the genus *Spiraea*, esp. *S. alba* or *S. latifolia*, of east North America, having pyramidal clusters of flowers.

mea·ger also **mea·gre** (mē'gər) *adj.* **1.** Having little fl can. **2.** Deficient in quantity, fullness, or extent; sca **3.** Deficient in richness, fertility, or vigor; feeble: *the mea soil of an eroded plain.* [ME *megre* < OFr. < Lat. *ma* **—mea'ger·ly** *adv.* **—mea'ger·ness** *n.*

Synonyms: *meager, spare, sparse, skimpy, scanty, sc Meager* indicates deficient supply, often of general or int plete requisites: *meager resources; meager education. Sp* implies bare sufficiency, free of all excess. It is often app to physical characteristics of persons (*spare of build*) and manner of speech or writing (*spare style*). *Sparse* indic lack of density and a spatial separation of units: *sparse v vegetation; sparse hair. Skimpy* emphasizes conspicuous sm ness or brevity: *a skimpy dress; a skimpy allowance. Sca* conveys the same sense, most often of physical ext many living quarters. *Scant* applies to what is barely eno or just short of a minimal amount: *a scant hour; a sc measure.*

meal[1] (mēl) *n.* **1.** The edible seed or other edible part grain, coarsely ground. **2.** A granular substance produ by grinding. [ME *meale* < OE *melu.*]

meal[2] (mēl) *n.* **1.** The food served and eaten in one sitt **2.** A customary time or occasion of eating food. [ME < *mēl.*]

mealie (mē'lē) *n. So. Afr.* **1.** An ear of corn. **2. meal** corn; maize. [Afr. *milie* < Port. *milho*, millet < Lat. *mili*

meal ticket *n.* **1.** A card or ticket entitling the holder t meal or meals. **2.** *Slang.* A person or thing depended on source of financial support.

meal·time (mēl'tīm') *n.* The usual time for eating a m

meal·worm (mēl'wûrm') *n.* The larva of any of several b forms of the genus *Tenebrio* that infest flour and other g products and are raised for bird feed.

mealy (mē'lē) *adj.* **-i·er, -i·est. 1.** Resembling meal in text or consistency; granular: *mealy potatoes.* **2. a.** Made o containing meal. **b.** Sprinkled or covered with meal c granular substance. **3.** Flecked with spots; mott **4.** Lacking healthy coloring; pale. **5.** Mealy-mouth **—meal'i·ness** *n.*

mealy·bug (mē'lē-bŭg') *n.* Any of various insects of the genus *Pseudococcus*, some of which are destructive to pla esp. citrus trees. [So called because it is covered with a w powdery substance.]

mealy-mouthed (mē'lē-mouthd', -moutht') *adj.* Unwill to state facts or opinions simply and directly.

mean[1] (mēn) *v.* **meant** (mĕnt), **mean·ing, means. 1. a.** To be defined or described as; denote: *The word "a means a certain species of mammal.* **b.** To convey the s sense as; refer to the same thing as: *The French w chien" means "dog."* **c.** To act as a symbol of; signify: *his poem, the budding flower means youth.* **2.** To intend convey or indicate: *What do you mean by that look?* **3.** here as a purpose or intention; intend: *"Most of the g who were not betrothed meant to be teachers"* (Sinc Lewis). **4.** To design or intend for a certain purpose or e a building *meant for storage.* **5.** To have as a consequen bring about: *Friction means heat.* **6.** To be attended by associated with: *Red sky at night means fair weather.* —i **7.** To be of a specified importance or significance; mat *The opinions of critics meant little to him.* **2.** To have in kind of a specified kind; be disposed: *She means well, over her blunders.* **—idiom. mean business.** *Informal.* To be earnest. [ME *menen* < OE *mǣnan*, to tell of.]

Synonyms: *mean, signify, import, denote, repres Import. Mean* is the least specific of the verbs conside

as for example, to distinguish *mid-den* (the
n) from the word *midden*. Note that the adjec-
ve is a separate word, though, as with any
ay be joined to another word with a hyphen
a unit modifier: *in the mid Pacific*, but *a mid-*

r') *n.* A point or region in the middle of the
ating in midair.
:) *n.* The fabled king of Phrygia to whom Dio-
: power of turning to gold all that he touched.

id'brān') *n.* **1.** The mesencephalon. **2.** The
›rain that develop from the midbrain region.
nid'kôrs', -kôrs') *n. Aerospace.* The part of a
t between burnout and re-entry, during which
neuvers are made.
'kŭlt') *n.* A form of intellectual and artistic
ıas qualities of both high culture and mass
ıt being either. [MID(DLEBROW) + CULT(URE)]
dā') *n.* The middle of the day; noon. *—modi-*
snack. [ME < OE *middæg* : *midd*, mid + *dæg*

'n) *n.* **1.** A dunghill or refuse heap, esp. of a
·itation. **2.** A kitchen midden. [ME *myddung*,
orig.]
!) *adj.* **1.** Equally distant from extremes or lim-
he middle point on a line. **2.** Being at neither
nor the other; intermediate. **3. a.** Intervening
:arlier and a later period of time; part of a
eries: *the middle years.* **b. Middle.** *Geol.* Desig-
ion between an earlier and a later division: *the*
zoic. **4. Middle.** Designating a stage in the de-
a language or literature between earlier and
Middle English. **5.** *Logic.* Designating a term
in both premises of a syllogism but not in the
. *Gram.* Of a verb form or voice in which the
performs and is affected by the action spec-
An area or point equidistant between extremes:
iddle of a circle. **2.** Something intermediate be-
es; mean. **3.** The interior portion: *the middle of*
The middle part of the human body; waist
niddle term. *—tr.v.* **-dled, -dling, -dles.** **1.** To
middle. **2.** *Naut.* To fold in the middle: *middle*
middel < OE.]
n. The time of human life between youth and
ally reckoned as the years between 40 and 60.
d (mĭd'l-ājd') *adj.* Of or pertaining to middle

: *pl.n.* The period in European history between
l the Renaissance, often dated from A.D. 476 to

rica *n.* **1.** That part of the U.S. middle class
s being average in income and education and
in values and attitudes. **2.** The American heart-
t of as being made up of small towns, small
ıburbs. **—Middle American** *n.*
v (mĭd'l-brou') *n. Informal.* One who is some-
d. **—mid'dle-brow'** *adj.*
Mus. The musical tone represented by the first
elow the treble clef or the first ledger line above

s *n.* The members of society occupying a socio-
›osition intermediate between the laboring
the wealthy.
is (mĭd'l-klās') *adj.* Of, pertaining to, or charac-
e middle class.
ance *n.* **1.** The area between the foreground and
in a painting, drawing, or photograph.
division of competition in racing with events
ging from 400 meters to 1,500 meters, or 440
ile.
ch *n.* The Dutch language from the middle of
ough the 15th century.
n. The space between the tympanic membrane
ernal ear, containing the auditory ossicles that
ations to the auditory tube.
lish *n.* The English language from about 1100 to

and *n.* **1.** Middle distance (sense 1). **2.** A point
way between extremes.
gh German *n.* High German from the 11th
15th century.
n *n.* Irish from the 10th through the 13th century.
r German *n.* Low German from the middle of
rough the 15th century.
n (mĭd'l-măn') *n.* **1.** A trader who buys from
and sells to retailers or consumers. **2.** An inter-
›-between.
nagement *n.* A group of persons occupying an
e managerial position below the level of upper
—middle manager *n.*
st (mĭd'l-mōst') *adj.* Midmost. [ME *middelmast*:
ldle + *-mast*, -most.]
the-road (mĭd'l-ɔv-thə-rōd') *adj.* **1.** Pursuing a
›tion midway between extremes, esp. following a
›olitics that is neither liberal nor conservative

: / g gag / h hat / hw which / ĭ pit / ī pie / ir pier /
ŏ paw, for / oi noise / ou out / o͝o took / o͞o boot /

2. Of, relating to, or being a type of popular music that appeals to a wide audience.

middle school *n.* A school that usually includes grades five through eight.

middle term *n.* The term in a syllogism presented in both premises but not appearing in the conclusion.

Mid-dle-town (mĭd'l-toun') *n.* A hypothetical community regarded as representative of Middle America.

mid-dle-weight (mĭd'l-wāt') *n.* A boxer or wrestler weighing between 147 and 160 pounds.

Middle Welsh *n.* Welsh from the 12th through the 15th century.

mid-dling (mĭd'lĭng, -lĭn) *adj.* **1.** Of medium size, position, or quality. **2.** Mediocre. *—n.* **1.** Often **middlings.** *Chiefly Southeastern U.S.* Pork or bacon cut from between the ham and shoulder of a pig. **2.** Any of various products that are intermediate in quality, size, price, or grade. **3. middlings** *(used with a sing. or pl. verb).* Coarsely ground wheat mixed with bran. *—adv. Informal.* Fairly; moderately. [ME *mydlyn* : *mid*, mid + *-ling*, small.] **—mid'dling-ly** *adv.*

mid-dy (mĭd'ē) *n., pl.* **-dies.** **1.** *Informal.* A midshipman. **2.** A middy blouse.

middy blouse *n.* A woman's or child's loose blouse with a sailor collar.

mid-field (mĭd'fēld') *n.* **1.** The section of a playing field midway between goals. **2.** Players on a team whose usual position is in the midfield. **—mid'field'er** *n.*

Mid-gard (mĭd'gärd') *n. Myth.* The part of the world inhabited by men, imagined as a fortress encircled by a huge serpent, built by the Norse gods around the middle region of the universe. [ON *Miðgarðr.*]

midge (mĭj) *n.* **1.** Any of various gnatlike flies of the family Chironomidae, found worldwide. **2.** A small person. [ME *migge* < OE *mycg.*]

midg-et (mĭj'ĭt) *n.* **1.** An extremely small person who is otherwise normally proportioned. **2.** A small or miniature version of something. **3.** A class of small objects, such as a class of very small sailboats or racing automobiles. *—adj.* **1.** Miniature; diminutive. **2.** Belonging to a type or class much smaller than what is considered standard: *a midget automobile.* [Dim. of MIDGE.]

mid-gut (mĭd'gŭt') *n.* The middle section of the digestive tract in the vertebrate embryo from which the ileum and the jejunum develop.

mid-i (mĭd'ē) *n.* A skirt or coat of mid-calf length. [< MIDDLE.]

Mid-i-an-ite (mĭd'ē-ə-nīt') *n.* One of the ancient Arabian tribe of Midian. **—Mid'i-an-ite'** *adj.*

mid-i-ron (mĭd'ī'ərn) *n.* An iron golf club that has more loft than a driver and less than a mashie, used for medium fairway shots and long approach shots.

mid-land (mĭd'lənd) *n.* The middle or interior part of a specific country or region. *—adj.* Of or in a midland.

mid-line (mĭd'līn') *n.* A medial line, esp. the medial line or plane of the body.

mid-most (mĭd'mōst') *adj.* **1.** Situated in the exact middle; middlemost. **2.** Situated nearest the middle. *—adv.* In the middle. [ME *midmest* < OE : *midd*, mid + *-mest*, -most.]

mid-night (mĭd'nīt') *n.* **1.** The middle of the night; specifically, 12 o'clock at night. **2. a.** Intense darkness or gloom. **b.** A period of darkness and gloom. *—modifier: a midnight swim; a midnight meeting; fell into a midnight mood from which nobody could rouse her.* **—idiom. burn the midnight oil.** To work or study very late at night. [ME < OE *midniht* : *midd*, mid + *niht*, night.]

midnight sun *n.* The sun as seen at midnight during the summer within the Arctic or Antarctic Circle.

mid-point (mĭd'point') *n.* **1.** The point of a line segment or curvilinear arc that divides it into two parts of the same length. **2.** A position midway between two extremes.

Mid-rash (mĭd'räsh') *n., pl.* **Mid-rash-im** (mĭd-rä'shĭm). Any of a group of Jewish commentaries on the Hebrew Scriptures written between A.D. 400 and 1200. [Heb. *midhrāsh*, commentary.]

mid-rib (mĭd'rĭb') *n.* The central or principal vein of a leaf.

mid-riff (mĭd'rĭf') *n.* **1.** The diaphragm (sense 1). **2.** The middle outer portion of the front of the human body extending roughly from just below the breast to the waistline. [ME *midrif* < OE *midhrif* : *midd*, mid + *hrif*, belly.] **—mid'riff'** *adj.*

mid-sec-tion (mĭd'sĕk'shən) *n.* A middle section, esp. the midriff of the human body.

mid-ship (mĭd'shĭp') *adj.* Of, pertaining to, or located in the middle of a ship.

mid-ship-man (mĭd'shĭp'mən, mĭd-shĭp'mən) *n.* **1.** A student training to be a commissioned naval officer, esp. a student at a naval academy. **2.** Any of various fishes of the genus *Porichthys*, having several rows of light-producing organs along their bodies.

mid-ships (mĭd'ships') *adv.* **1.** Amidships. **2.** In the center position. Used of the helm. [Short for AMIDSHIPS.]

midst (mĭdst, mītst) *n.* **1.** The middle position or part; center: *in the midst of the desert.* **2.** A position of proximity to other individuals or members: *a stranger in our midst.* **3.** The condition of being surrounded by or beset by something: *in the midst of all of our problems.* **4.** A time period about the middle of a continuing condition or act: *in the midst of the war.* *—prep.* Among. [ME *middest*, alteration of *middes* < *midde*, in the middle < OE, middle.]

mid-stream (mĭd'strēm') *n.* **1.** The middle part of a stream. **2.** The middle part of a course that is neither at the beginning nor at the end: *the midstream of life.*

mid-sum-mer (mĭd'sŭm'ər) *n.* **1.** The middle of the summer. **2.** The summer solstice, about June 21. **—modifier:** *a midsummer night.*

Midsummer Day *n.* The feast of the birth of John the Baptist, celebrated June 24.

mid-term (mĭd'tûrm') *n.* **1.** The middle of an academic term or a political term of office. **2. a.** An examination given at the middle of a school term. **b. midterms.** A series of such examinations.

mid-town (mĭd'toun') *n.* A central portion of a city, located between uptown and downtown.

mid-Vic-to-ri-an (mĭd'vĭk-tôr'ē-ən, -tōr'-) *adj.* Pertaining to, occurring in, or characteristic of the middle period of the reign of Queen Victoria in Great Britain (1837–1901), a period known for rigid social standards. *—n.* **1.** A person living in the mid-Victorian period. **2.** A person having mid-Victorian ideas.

mid-way (mĭd'wā') *n.* **1.** The area of a fair, carnival, circus, or exposition where side shows and other amusements are located. **2.** *Obs.* **a.** The middle of a way or distance. **b.** A middle way or course of action or thought. *—adv.* In the middle of a way or distance; halfway. **—mid'way'** *adj.*

mid-week (mĭd'wēk') *n.* The middle of the week. **—modifier:** *a midweek appointment with the dentist.* **—mid'week'ly** *adj. & adv.*

mid-wife (mĭd'wīf') *n.* **1.** A woman who assists women in childbirth. **2.** One who assists in bringing something about. *—tr.v.* **-wifed** or **-wived** (-wīvd'), **-wif-ing** or **-wiv-ing** (-wī'vĭng), **-wifes** or **-wives** (-wīvz'). To assist in bringing forth or about. [ME *midwif* : *mid*, with (< OE) + *wif*, woman < OE *wīf.*]

mid-wife-ry (mĭd'wīf'rē, -wī'fə-rē, mĭd-wīf'ə-rē) *n.* The techniques and practice of a midwife.

mid-win-ter (mĭd'wĭn'tər) *n.* **1.** The middle of the winter. **2.** The period of the winter solstice, about December 22. **—modifier:** *a midwinter day.*

mid-year (mĭd'yĭr') *n.* **1.** The middle of the calendar or academic year. **2. a.** An examination given in the middle of the school year. **b. midyears.** A series of such examinations.

mien (mēn) *n.* **1.** Bearing or manner; expression: *a person of noble mien.* **2.** An appearance or aspect. [< DEMEAN.]

miff (mĭf) *n.* **1.** A petulant, bad-tempered mood; huff. **2.** A petty quarrel or argument; tiff. *—tr.v.* **miffed, miff-ing, miffs.** To cause to become offended or annoyed. [Orig. unknown.]

mif-fy (mĭf'ē) *adj.* **-fi-er, -fi-est.** **1.** *Informal.* Easily offended; oversensitive. **2.** *Bot.* Difficult to raise except under perfect conditions. Used of certain plants. **—mif'fi-ness** *n.*

might[1] (mīt) *n.* **1.** Tremendous power, force, or influence: *the might of the allied armies.* **2.** Physical or bodily strength. **3.** Strength or ability to do something: *tried with all her might.* [ME < OE *miht.*]

might[2] (mĭt) *aux.v.* **1. a.** Used to indicate a condition or state contrary to fact: *She might help if she knew the truth.* **b.** Used to indicate a possibility or probability that is weaker than *may*: *We might discover a pot of gold at the end of the rainbow.* **2.** Used to express possibility or probability or permission in the past. **3.** Used to express a higher degree of deference or politeness than *may*: *Might I express my opinion?* [ME < OE *meahte*, 1st and 3rd person p. indicative of *magan*, to be able.]

Usage: In many Southern varieties of English, *might* is used in the "double modal" construction with *could*, as in *We might could park over there.* Less frequently, one hears *may can* and *might should.* These constructions are not familiar to the majority of American speakers and are best avoided in formal writing.

might-i-ly (mī'tl-ē) *adv.* **1.** In a mighty manner; powerfully. **2.** To a great degree; greatly.

might-y (mī'tē) *adj.* **-i-er, -i-est.** **1.** Having or showing great power, skill, strength, or force: *a mighty orator; a mighty blow.* **2.** Imposing or awesome in size, degree, or extent: *a mighty stone fortress.* *—adv. Informal.* To a great degree; extremely. **—might'i-ness** *n.*

mi-gnon-ette (mĭn'yə-nĕt') *n.* A plant, *Reseda odorata*, native to the Mediterranean region and widely cultivated for its clusters of fragrant but inconspicuous greenish flowers. [Fr., fem. of obs. *mignonnet*, dim. of *mignon*, dainty.]

mi-graine (mī'grān') *n.* Severe, recurrent headache, usually affecting only one side of the head, characterized by sharp pain and often accompanied by nausea. [ME < OFr. < LLat. *hemicrania*, pain in one side of the head < Gk. *hēmikrania* : *hemi-*, half + *kranion*, head.] **—mi'grain-ous** *adj.*

mi-grant (mī'grənt) *n.* **1.** One that moves from one region to another by chance, instinct, or plan. **2.** An itinerant worker who travels from one area to another in search of work. *—adj.* Migratory. [Lat. *migrans, migrant-*, pr.part. of *migrare*, to migrate.]

mi-grate (mī'grāt') *intr.v.* **-grat-ed, -grat-ing, -grates.** **1.** To move from one country or region and settle in another. **2.** To change location periodically, esp. to move seasonally

midget

migrant

p pop / r roar / s sauce / sh ship, dish / t tight / th thin, path / *th* this, bathe / ŭ cut / ûr urge / v valve / w with / y yes / z zebra, size / zh vision / ə about, item, edible, gallop, circus / œ *Fr.* feu, *Ger.* schön / ü *Fr.* tu, *Ger.* über / KH *Ger.* ich, *Scot.* loch / N *Fr.* bon.